21 CFR Part 11 –
A Risk Management Perspective

November 13, 2003

PRICEWATERHOUSECOOPERS

Proposed Agenda

- 21 CFR Part 11 Baseline
- Recent 21 CFR Part 11 Developments
- Integration with other Legislation
- Lessons Learned
- Risk Management Perspective
- An Example
- Considerations

21 CFR Part 11 Baseline

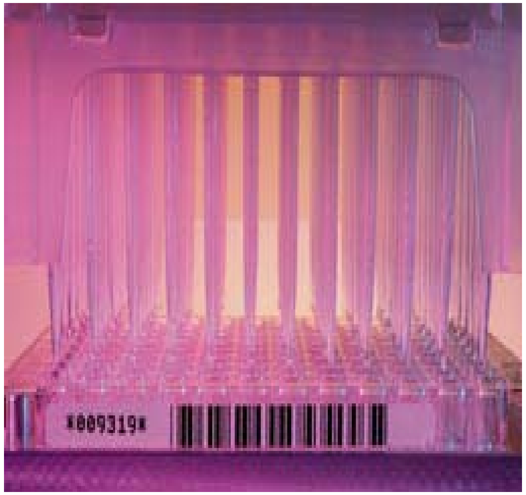
- **Regulation Established August 1997**
- **"All required controls that make e-record keeping trustworthy, reliable and compatible with FDA role", *Paul Motisse***
- **The controls that were in place for paper records and handwritten signatures translated to an electronic environment**
- **Control Requirements:**
  - Security
  - Archiving
  - Audit Trails
  - Copy Controls
  - Sequencing Controls
  - Device Checks
  - Change Control
  - Document Control
  - Computer Systems Validation

Recent Developments

- **All previous Part 11 guidance has been withdrawn**
- **New final guidance has been provided**
- **Final guidance acknowledges that:**
  - Statements made by agency staff may have been misinterpreted as policy
  - The use of technology has been restricted, contrary to the agency’s intent
  - The cost of compliance far exceeds the agency’s expectations
  - Part 11 has discouraged innovation without a significant public health benefit

Recent Developments

- Part 11 is being re-examined and may be revised
- Certain areas will be subject to enforcement discretion (validation, audit trails, record retention and record copying)
- All other areas will continue to be enforced
- Narrow Scope – Part 11 applies when persons choose to use records in electronic format in place of paper records
- Decisions to rely on paper or electronic records should be documented



Recent Developments

- **There are wide ranging opinions regarding what these changes mean**
- **Key messages:**
  - Part 11 is not going to go away
  - One size does not fit all
  - Focus on risk management – an effective internal control structure that protects product safety, quality and efficacy

Integration with Other Legislation – Connected Thinking

- Annex 11
- EPA
- HIPAA
- State Privacy Law
- EU Data Protection Direction
- ISO
- Basel II Accord
- Cadbury Turnbull
- Sarbanes-Oxley

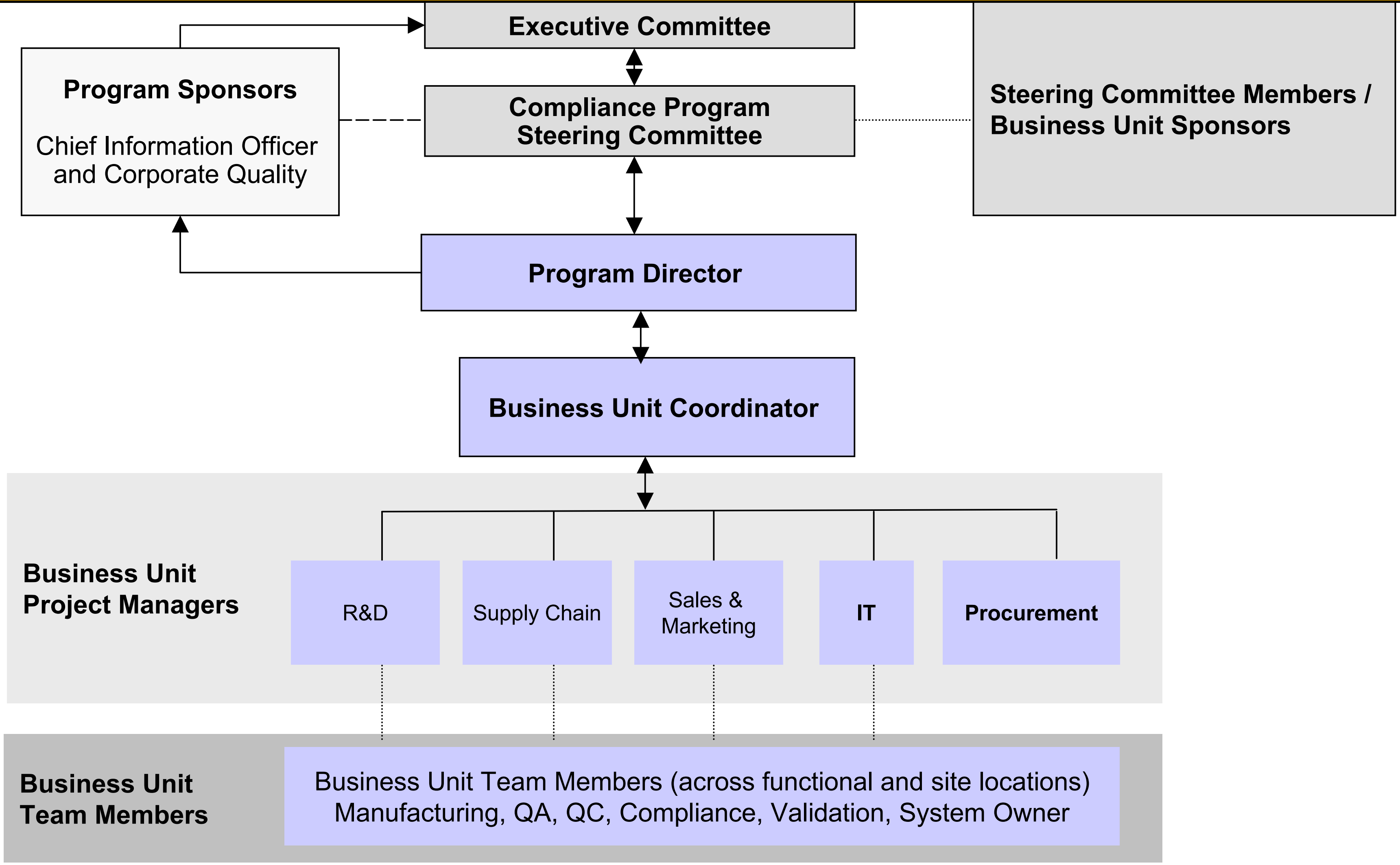
Where are They Similar and Different?

	FDA	21 CFR Part 11	EPA	Annex 11	HIPAA	Sarbanes-Oxley
Security Organization		X			X	X
Audit Trails		X	X	X		X
Electronic Signatures		X	X			
Archiving		X	X			
Validation	X	X		X		X
Backup and Recovery		X		X		X
Record Retention	X	X		X		
Disaster Recovery Planning		X		X		X
Access Controls		X	X	X	X	X
Training	X			X		X

Lessons Learned – Key Challenges

- **How does Part 11 rank in importance to other business priorities and regulations?**
- **What are acceptable remediation timeframes? Who decides?**
- **What does the final guidance mean given where my Company is in the process?**
- **How do we embed compliance into the business and system development lifecycle?**
- **How do we realize value from this compliance initiative?**

Example Program Structure



Executive Committee

Program Sponsors

Chief Information Officer and Corporate Quality

Compliance Program Steering Committee

Steering Committee Members / Business Unit Sponsors

Program Director

Business Unit Coordinator

Business Unit Project Managers

R&D

Supply Chain

Sales & Marketing

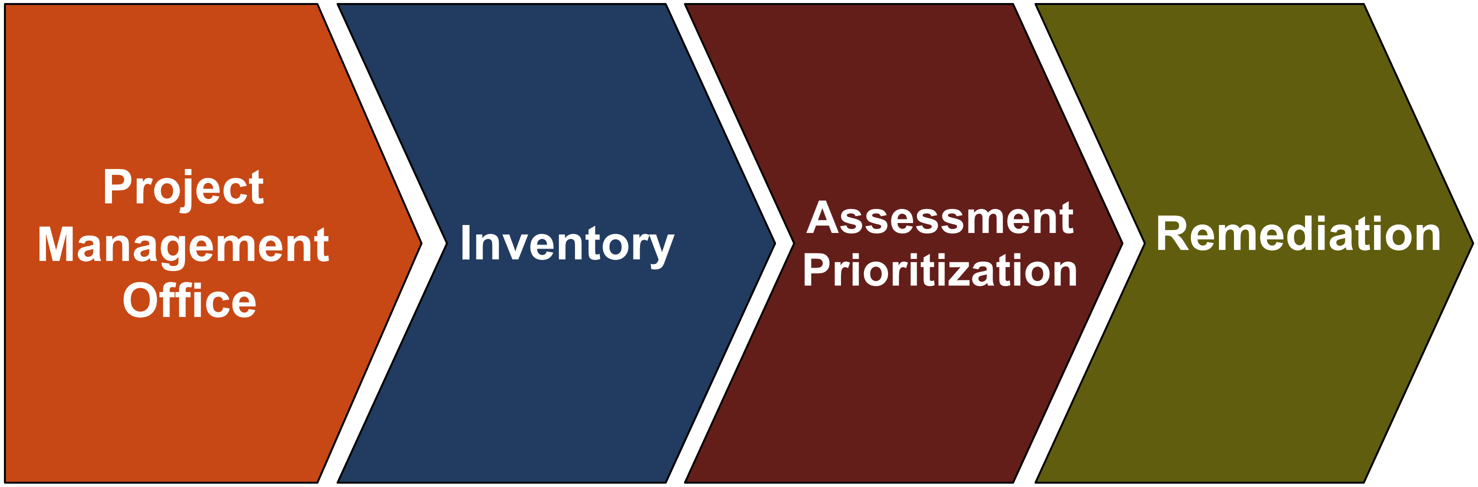
IT

Procurement

Business Unit Team Members

Business Unit Team Members (across functional and site locations)
Manufacturing, QA, QC, Compliance, Validation, System Owner

Compliance Program Office



Project Management Office

Inventory

Assessment Prioritization

Remediation

Lessons Learned

- **Executive Sponsorship**
  - Information Technology
  - Quality Assurance
  - Business Leadership
  - Steering Committee
  - Active Involvement

- **Roles and Responsibilities**
  - Program Management
  - Business
  - Information Technology
  - Quality Assurance
  - Validation
  - Internal/External Audit

- **Program Management**
  - Project Planning
  - Risk and Issue Management
  - Templates, Processes and Procedures
  - Training
  - Monitoring
  - Reporting
  - Financial Management
  - Stakeholder Management
  - Portfolio Prioritization
  - Benefits Realization
  - Transition Plan

Lessons Learned

- **Overlooked Areas**
  - Technology Infrastructure
  - Procurement Process
  - Third Parties (Vendors, Suppliers, etc.)
  - Standard Operating Procedures
- **Inventory Process**
  - Methodology
  - Training
  - Monitoring
  - Change Control
  - Ownership
- **Assessment Process**
  - Methodology
  - Linkage to Remediation Plan and Requirements
  - Training
  - Monitoring
  - Change Control
  - Compliance Score

Lessons Learned

- **Prioritization**
  - Determine risk profile:
    - Compliance Score
    - System Lifecycle Stage
    - Inspection History (Company and Industry)
    - Impact on Quality, Safety, Efficacy, financial statements, operational objectives
    - Complexity
    - Standalone vs. Networked
    - Customized vs. Off-the-Shelf
  - Identity Common Systems and Consolidation Targets
  - Identify preliminary remediation approach (repair, replace or procedural)
  - Calculate Budget
  - Establish Compliance Based Remediation Targets and Timelines
  - Confirm prioritization with relevant stakeholders
  - Capture Benefits

Lessons Learned

- **Remediation - Risk Assessment**
  - Focus on Business Process
  - Everything is not important – only those things that impact quality decisions
  - Product quality, safety and efficacy
  - Data Integrity, Confidentiality and Availability
  - An Risk Based Approach
    - Analyze Business Process
    - Understand Quality Related Objectives
    - What are the risks that could impact the objectives?
    - What controls must be established to mitigate the risks?
    - Controls become requirements
    - Validation provides evidence that the controls are in place and operating effectively

Procurement - Example

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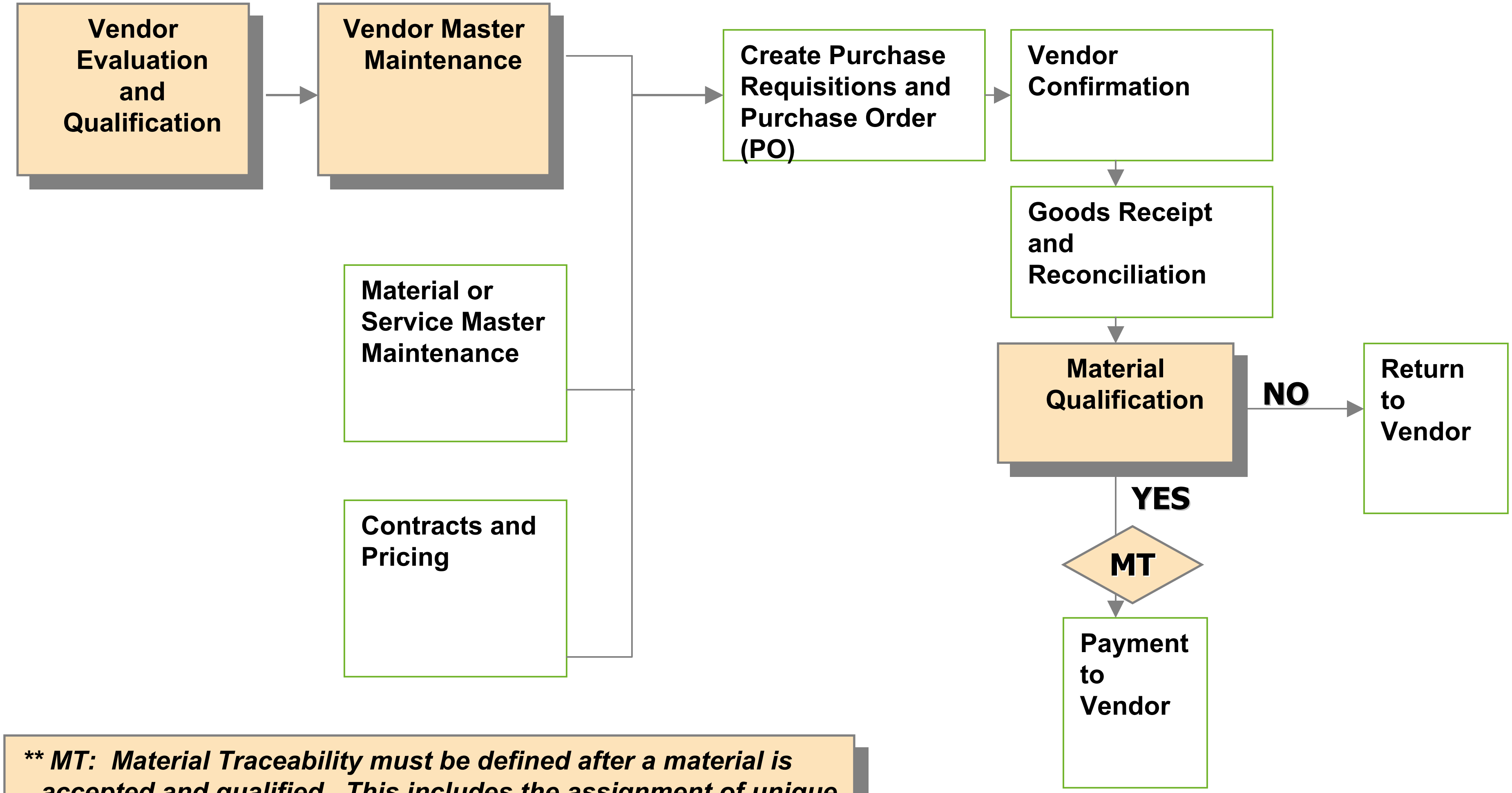
Procurement & Vendor Qualification



Vendor Evaluation and Qualification

Vendor Master Maintenance

Material or Service Master Maintenance

Contracts and Pricing

Create Purchase Requisitions and Purchase Order (PO)

Vendor Confirmation

Goods Receipt and Reconciliation

Material Qualification

NO

Return to Vendor

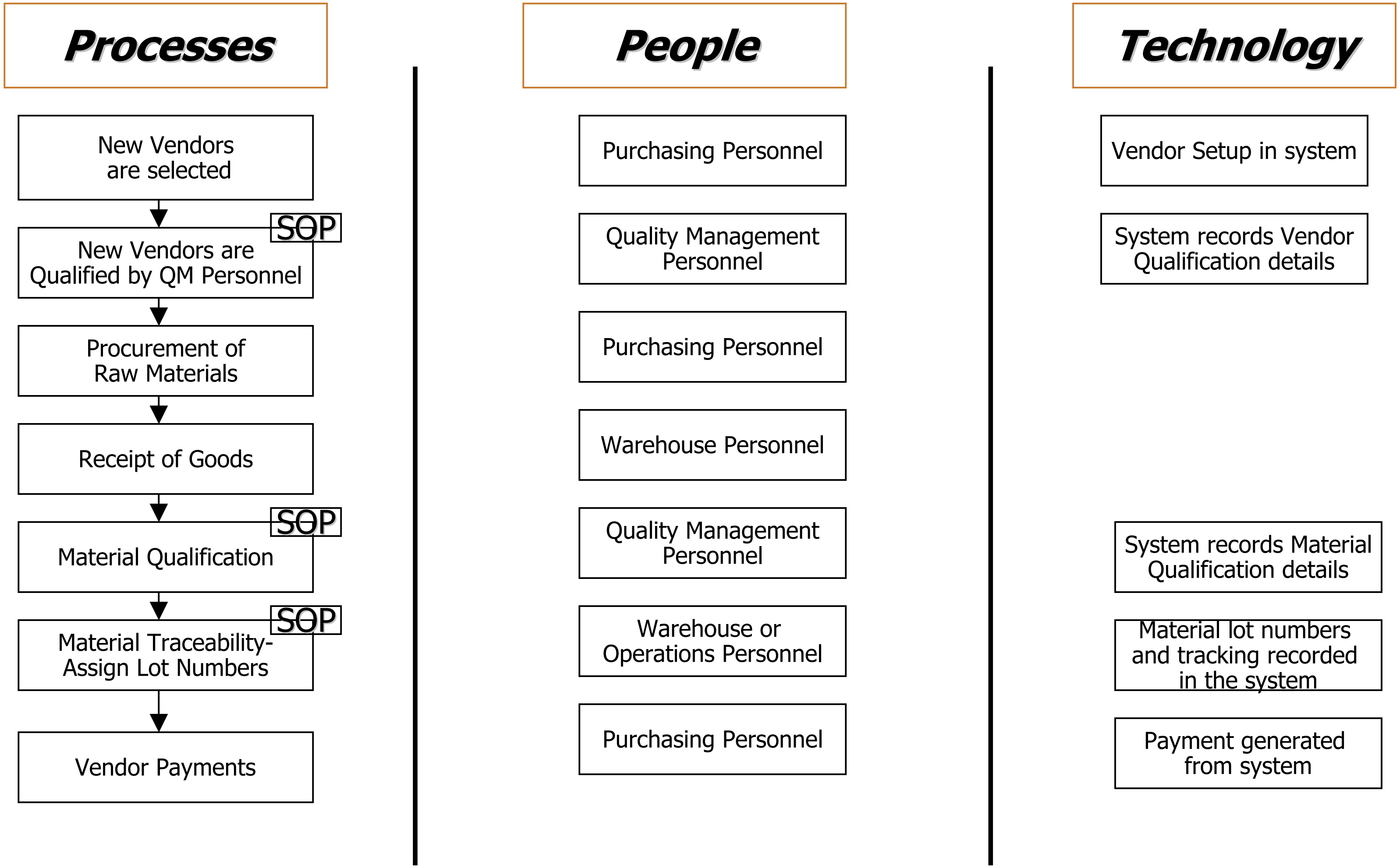
YES

MT

Payment to Vendor

***** MT: Material Traceability must be defined after a material is accepted and qualified. This includes the assignment of unique lot numbers after receipt at a manufacturing site. *****

People, Process and Technology



Processes	People	Technology
New Vendors are selected	Purchasing Personnel	Vendor Setup in system
SOP New Vendors are Qualified by QM Personnel	Quality Management Personnel	System records Vendor Qualification details
Procurement of Raw Materials	Purchasing Personnel	
Receipt of Goods	Warehouse Personnel	
SOP Material Qualification	Quality Management Personnel	System records Material Qualification details
SOP Material Traceability- Assign Lot Numbers	Warehouse or Operations Personnel	Material lot numbers and tracking recorded in the system
Vendor Payments	Purchasing Personnel	Payment generated from system

Example

ID No.	Process	Risk	COSO Component	COSO Control Objective	COSO Control Objective Category (C,F,O)	Control Type (C,A, V,R)	Control Requirements
1	Vendor Maintenance	Changes to standing data are not completely and accurately input increasing the risk of improper payment to unauthorized or incorrect suppliers.	Control Activity	Changes to standing data are completely and accurately input.	Operational Financial	C,A	1) On-line edit and validation checks exist in the payables system to verify the accuracy of key vendor master data fields are entered. 2) 2) Key data fields are required during vendor maintenance. 3) The system will check for duplicate vendor names, addresses, or other key data fields and flag the transaction for review before processing further.
2	Vendor Maintenance	Purchase orders are released with an invalid material vendor combination resulting in material that is purchased from an unqualified vendor	Control Activity	Vendors are qualified before updating the vendor master file	Operational Compliance (CFR 820.50 (a) (3))	C, A, V	1) Vendor Qualification SOP is in place, approved and effective 2) Vendor master controls shall be established to prevent sourcing materials to vendors that are not qualified

Considerations

- How connected are your Company's efforts with respect to addressing related regulations?
- Does your Company have a consistent point of view regarding the appropriate level of compliance and associated documentation?
- Does your Company have a consistent risk management approach to focus compliance efforts?
- Are risk based decisions documented and linked to the compliance approach?
- Does your Company have a process to prioritize processes, systems and compliance projects based on risk?
- Does your Company have a system development lifecycle and validation methodology that is focused on key risk areas to assure compliance objectives?